

University of Groningen

In memoriam Enno Mandema, MD (1921-2010)

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In memoriam Enno Mandema, MD (1921-2010)

Bouke P. Hazenberg, Erik Gruys, & Martin H. van Rijswijk

Course of life

Enno Mandema studied Medicine from 1939–1948 in Groningen in the Netherlands and became internist in 1954. Two years later, he defended his PhD thesis *summa cum laude*. In 1959, he visited professor Robert M. Kark in Chicago during 1 year for research on the antinuclear factor, SLE, and proteins. In 1960, 38 years old, he became full professor of Medicine and head of Department of Medicine in Groningen. Together with Bob Nienhuis, he discovered the anti-perinuclear factor in patients with rheumatoid arthritis in 1963. In 2000, almost 40 years later, this serendipitous discovery turned out to be the anti-CCP, a very specific auto-antibody in rheumatoid arthritis. In 1975, he became Honorary Fellow of the American College of Physicians and in 1979 Member of The Royal Netherlands Academy of Arts and Sciences. In 1986, Dr. Mandema retired and this was celebrated with an International Course on Amyloidosis in Groningen, organized by Jan Marrink and Martin van Rijswijk. After his retirement, he became the first President of the Dutch Council for Health Research until 1993 and advised the Dutch Government in three major reports. He was honored by Queen Beatrix and became Knight in the order of the “Nederlandse Leeuw”. Subsequently, he became the Queen’s Chamberlain for the Province of Groningen. In 2009, the University Medical Center of Groningen founded a “Mandema stipendium”, a grant for stimulation of research performed by promising young physicians.

Amyloidosis research

In his thesis in 1956, Dr. Mandema focused his research on patients with multiple myeloma and Waldenström’s disease. Some of his patients suffered also from amyloidosis and he became fascinated by the disease. He saw great opportunities for clinical and biochemical research in this area. Together with Jan Scholten, Luuk Ruinen and Alan Cohen he organized the first International Symposium on Amyloidosis in Groningen in 1967. This Symposium marked the start of

an era of international collaboration with huge progress of amyloidosis research leading to better understanding of the disease and improvement of patient care, treatment, and outcome. An independent scientific journal and a supportive society also mark the growing independence and relevance of this research area.

In the Netherlands, amyloidosis research started around 1980 as reflected in the PhD theses of Erik Gruys, in Utrecht in 1979, and Martin van Rijswijk, in Groningen in 1981. In Groningen, Martin van Rijswijk, Jan Marrink, and Sijtze Meijer coached Sven Janssen (PhD 1985) in clinical studies of precursor proteins, e.g. SAA and M-proteins, histology (KMnO₄) and immunohistochemistry, therapy (“precursor-product” concept, DMSO), and clinimetry (cohort studies, kidney function, bone scintigraphy, and cardiac ultrasound). Subsequently, Martin van Rijswijk and Pieter Limburg coached Bouke Hazenberg (PhD 2007), Ingrid van Gameren (PhD 2009), and Johan Bijzet in clinical studies focusing on the role of subcutaneous fat tissue and SAP scintigraphy in diagnosis, clinimetry, and monitoring of therapy.

In Utrecht, Erik Gruys coached Paul Hol and Adriaan van Anel in veterinary studies of AA amyloidogenesis in Syrian hamsters, cattle, and dogs with a focus on SAA and SAP. Localized AL amyloidosis was discovered in the horse. Subsequently, Erik Gruys coached Theo Niewold (PhD 1990) in his studies of AEF in AA amyloidosis in hamsters and cattle, Yves Goffin (PhD 1989) in his studies of amyloid in human heart valves and joints, Wil Landman (PhD 1998), Bereket Zekarias (PhD 2003), and Narin Upgarin (PhD 2005) in their studies of GAGs, SAA, AA amyloid, amyloid arthropathy, and inflammation in chickens, and Jaime Rofina (PhD 2005) in his studies of cerebral Alzheimer-like amyloid in aged dogs.

Some spin-off was visible outside the amyloidosis area: Martin van Rijswijk coached Miek van Leeuwen in her studies of the effect of CRP and SAA on progression of rheumatoid arthritis and Erik Gruys coached S Alsemgeest and Mathilda Toussaint in their studies of CRP, SAA, and haptoglobin in small domestic animals.

Epilogue

Enno Mandema always enjoyed attending the amyloidosis symposia and the contacts with so many amyloid friends. He was respected broadly for his knowledge, his dedication to his patients, his interest in medical science, and his clear view and opinions. Besides, he was a good teacher and colleague. His sight diminished slowly in the last years, but it was amazing how he compensated for this handicap. At all amyloidosis symposia he remained deeply interested in the program. He frequently asked us relevant questions about all kinds of presentations— and it was often not easy to provide a satisfactory answer. In 2006, he was not able to attend the Symposium in Woods Hole because of illness of his beloved wife Atie. At the end of 2008, he asked us to contact him in the beginning of 2010 to learn whether he would feel well enough to visit Rome in April. It turned out to be different. In the night of 27 January 2010, he passed away in his sleep at the blessed age of 88. We will remember him as a warm, congenial person and a good amyloid friend.



Figure 1. Enno Mandema together with his wife Atie in their garden in 1986.

Bouke P. Hazenberg, Groningen
Erik Gruys, Utrecht
Martin H. van Rijswijk, Groningen